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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,155	11/25/2003	Theodore R. Sana	10030511-1	8586

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/722,155	SANA ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *10-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 November 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/23/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-9 in the reply filed on July 31, 2006 is acknowledged.

However, Applicants do not appear to point out any supposed error made in making the restriction requirement, but rather, appear to discuss at length, the definition of restriction and how it pertains to the restricted claims.

While there no arguments to address in Applicants' response to the restriction requirement, Applicants make some generalization regarding restriction requirement that is incorrect. These will be pointed out herein.

Applicants state that art (if such art exists) indicating that the invention of one of the groups is known or would have been obvious would not extend to a holding that the invention of the other groups are known or would have been obvious (page 2, bottom paragraph, Response).

This statement is **fundamentally flawed** because the test for obviousness is whether the **claims** are obvious over each other, **not** whether the prior art can render obvious claims drawn to two inventions.

Certainly, there would be instances when claims would not be obvious over each other, but a piece of prior art holding obvious over one invention, in combination of other prior art teachings, can hold the other invention also obvious.

For example, consider a restriction requirement which restricts a method of fabricating an array, an array made therefrom (i.e., a product), and a method of using the array to diagnose breast cancer based on a known marker on said array.

The inventions are patentably distinct because the array, while fabricated by the method claims does not result in any physical distinction from the array produced by other means. In addition, a method of diagnosing breast cancer is not dependent on the method of fabrication nor the claims drawn to an array which is claimed generically.

It is clear that an array capable of holding its own patent (based on its physical elements) from a method of fabricating an array (based on the steps employed in the method), and from a method of diagnosing breast cancer (based on the steps employed in the method) – that is to say, three groups would be separately patentable over each other (i.e., patentably distinct – capable of holding separate patents).

Now, consider that a piece of prior art discloses an array which comprises the known marker. However, the art does not disclose that the array could be used in a breast cancer diagnosis.

However, there is another piece of prior art which teaches that the marker is associated with breast cancer.

Clearly, in view of the prior art, one is capable of holding obvious the method of diagnosing breast cancer using an array by combining the two pieces of prior art, and this without violating the rules of restriction.

The requirement is still deemed proper and is therefore made FINAL.

Claims 10-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on July 31, 2006.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any

amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

The IDS received on February 23, 2004 is acknowledged.

With regard to reference, U.S. Patent No, 0,124,588, it is determined that this reference cannot be considered since the reference retrieved is not issued to Wolber et al.

The same is determined fro references, U.S. Patent No. 0,009,608; 0,005,614; 0,002,072; 0,143,756; 0,143,329; and 0,112,295.

A signed copy of the PTO-1449 is enclosed herein.

Applicants must file a separate IDS with the correct citation of the patent numbers if Applicants desire said patents to be considered for the record.

Drawings

The drawings received on November 25, 2003 are acceptable.

Claim Interpretation

The phrase, "degenerate biopolymers," has been interpreted as disclosed by the instant specification:

> **[0032]** The phrase "degenerate biopolymers" refers to biopolymers that comprise one or more sites of degeneracy, for example, less than 10, less than 5, less than 3, or less 2 such sites. A site of degeneracy generally comprises a contiguous stretch of 1 to 5 nucleotides in length, one to 4 nucleotides in length, one to 3 nucleotides in length, one to 2 nucleotides in length, one nucleotide in length. The nucleotides of the degenerate sites are degenerate nucleotides where the nucleotide(s) of a respective degenerate site differ from nucleotide(s) in corresponding positions of another biopolymer, the biopolymers being otherwise generally of the same sequence composition. The nature and number of nucleotides in a degenerate site are generally determined by the nature of related sequences in a target sample whether the composition of such target sample is known or unknown.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of synthesizing a plurality of biopolymers at a predetermined locations of a surface of a substrate, wherein one or more of said feature locations comprises degenerate biopolymers, wherein said biopolymers are nucleic acid (i.e., polynucleotide, oligonucleotide), does not reasonably provide enablement for the method wherein said degenerate biopolymers are polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation are summarized in In Re Wands (858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)). They include (A) the quantity of experimentation necessary, (B) the amount of direction or guidance

presented, (C) the presence or absence of working examples, (D) the nature of the invention, (E) the state of the prior art, (F) the relative skill of those in the art, (G) the predictability or unpredictability of the art, and (H) the breadth of the claims.

Breadth of Claims:

Claims are broadly drawn to encompass that the method fabricates, on at least one or more feature of a surface of a substrate, a degenerate polypeptide.

Nature of the Invention & Amount of Guidance:

The instant specification gives a wholly generic definition in what is regarded as a biopolymer that is degenerate, in that such biopolymer is, "generally of the same sequence composition," other than that the degenerate nucleotides therein are "different." (see section [0032]).

Such definition reads on a method of generating an array of detecting single point mutations which comprises biopolymers which is, "generally of the same sequence composition," other than the "degenerate nucleotides" at the site of degeneracy, wherein the nucleotides are "different."

According to the definition widely accepted in the art, the term, "degenerate," in context of biopolymers is refers to a nucleic acid sequence which encodes the same protein, whose sequence maybe different.

As defined by A Dictionary of Genetics, 5th edition, the term, "degenerate code," is defined as:

> "one in which each different word is coded by a variety of symbols or groups of letters. The genetic code is said to be degenerate because more than one nucleotide triplet codes for the same amino acid."

Hence, when the degenerate biopolymer is drawn to a polypeptide, it become unclear just what nature of a polypeptide is to be "degenerate." Clearly, a polypeptide that is differing in amino acid is not "degenerate."

Based on such lacking teachings in the art or in the specification, one of skill in the art would clearly not be able to practice the claimed method fully commensurate in scope of the claims (i.e., method of synthesizing a plurality of biopolymers, wherein one or more of feature locations of a substrate comprises degenerate polypeptides) without undue experimentation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-7 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Cronin et al. (U.S. Patent No. 6,027,880, issued February 22, 2000, filed October 10, 1995, priority October 26, 1993).

Cronin et al. disclose a method of synthesizing a cystic fibrosis mutation chip which comprises a plurality of oligonucleotides immobilized at a predetermined locations, wherein said array comprises a reference sequence tiled thereto, followed by the tiling of the subgroups of oligonucleotides which comprises the same sequence as that of the reference oligonucleotide sequence excepting that said subgroups of oligonucleotides comprises at least one nucleotide that is

different from the reference sequence (i.e., interrogation position) (Figures 1 and 5; column 2, lines 43-49; column 3, lines 36-40; column 11, lines 24-28, 33-35, and 42-46).

Cronin et al. disclose that the array is fabricated via photolithography, which comprises the steps of providing nucleotide monomers onto an array substrate, said monomers being blocked at their 5'-OH ends with photoremovable blocking group, followed by their deprotection via mask-mediated photolithography (thus activation). The processes are repeated subsequent to the deprotection steps, so as to fabricate the array (column 52, lines 13-28), thereby clearly anticipating claims 1-7.

With regard to claim 9, the photolithography is mediated via computerized process (column 54, lines 14-18).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Cronin et al. (U.S. Patent No. 6,027,880, issued February 22, 2000, filed October 10, 1995, priority October 26, 1993) in view of Baldeschwieler et al. (WO 95/25116, published September 21, 1995).

The teachings of Cronin et al. have already been discussed above.

Cronin et al. do not explicitly disclose that the method of synthesizing the array involve a dispenser comprising at least one droplet dispensing device.

Baldeschwieler et al. disclose a method of synthesizing an array via use of an inkjet technology, wherein the method involves the attachment of molecules onto a substrate surface (page 1, lines 23-25), for sequential synthesis of polynucleotides (page 2, lines 1-3), wherein the reagents are dispensed from a microdrop dispensing device (page 3, lines 14-15).

The artisans teach the deprotection step (i.e., activation of the protected monomers) so as to "grow" the nucleotides thereto (page 4, lines 1-20).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Cronin et al. with the teachings of Baldeschwieler et al., thereby arriving at the claimed invention for the following reasons.

The art of microarray is replete with different types of fabrication methods, such as photolithographic method (as employed by Cronin et al.), capillary deposition (developed by Pat Brown), inkjet deposition (as employed by Baldeswieler et al.), etc.

Hence, one of ordinary skill in the art at the time the invention was made would have been motivated to employ any of the well known methods of fabrication microarray, such as that of Baldeschwieler et al., for fabricating the array disclosed by Cronin et al.

In addition, it is also clearly known that the photolithographic method of fabricating a microarray is costly, as a plurality of mask must be employed for fabricating a single type of array.

Hence, one of ordinary skill in the art at the time the invention was made would have been further motivated to find a more cost-efficient alternative technology, such as that of Baldeschwieler et al., thereby arriving at the claimed invention.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hanks et al. (Methods in Enzymology, 1991, vol. 200, pages 525-532) in view of Baldeswieler et al. (WO 95/25116, published September 21, 1995).

Hanks et al. disclose a method of using degenerate oligonucleotides probes so as to identify clones that encode protein kinases (page 525, 3rd paragraph).

The artisans recite the importance in being able to identify proteins of known functions which have not yet been discovered (page 525, 1st paragraph; in the phrase, "[t]he identification and characterization of novel protein kinases should lead to new insights into how cells regulate their activities").

The artisans disclose a known method of identifying homologous nucleic acids via low-stringency hybridization condition (page 525, 2nd paragraph), and in this context, disclose a "new" way of identifying homologous sequences (page 525, 3rd paragraph).

The artisans explicitly disclose that degenerate oligonucleotide probes are employed in a hybridization assay, wherein said degenerate oligonucleotide probes are designed to recognize target sequences that encode short stretches of six to nine highly conserved amino acid residues found within the catalytic domains (page 525, 3rd paragraph).

The artisans disclose that, "virtually all of the codon possibilities for a conserved stretch can be included in the probe mixture, thereby assuring that many different protein kinase genes (cDNAs) will be recognized." (page 525, 3rd paragraph).

Hanks et al., however, employ the degenerate oligonucleotides in an in-solution assay via radioactive labeling (page 529).

Baldeschwieler et al. disclose a method of synthesizing an array via use of an inkjet technology, wherein the method involves the attachment of molecules onto a substrate surface (page 1, lines 23-25), for sequential synthesis of polynucleotides (page 2, lines 1-3), wherein the reagents are dispensed from a microdrop dispensing device (page 3, lines 14-15).

Baldeschwieler et al. disclose the step-by-step addition of protected monomers, followed by the washing of uncoupled monomers, followed by the deprotection step (or activation), followed by the repeat of the addition of second protect monomers (page 4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Hanks et al. with the teachings of Baldeswiechler et al., thereby arriving at the invention as claimed for the following reasons.

The art of microarray technology has been well-established, wherein its advantage of allowing simultaneous detection of a plurality of (thousands) of target analytes is widely known and accepted.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to fabricate a microarray comprising a plurality of degenerate oligonucleotide probes (of Hanks et al.), for the well known benefit of simultaneously identifying a plurality of homologous genes of interest.

Given the fact that Hanks et al. gave all the necessary guidance for generating degenerate oligonucleotide probes for identifying related genes; whereby coupled with the teachings of Baldeswiechler et al. who gave all the necessary guidance for fabricating an array via use of a dispenser, one of ordinary skill in the art, at the time the invention was made, would have had a reasonable expectation of success at combining the teachings so as to arrive at the method of fabricating on a solid substrate, a plurality of degenerate oligonucleotide probes.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent

to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Young J. Kim
Primary Examiner
Art Unit 1637
9/11/2006

YOUNG J. KIM
PRIMARY EXAMINER

YJK